Summary of Safety and Effectiveness Data (SSED)
EXCLUDER™ Bifurcated Endoprosthesis

1.0 General Information

Device Generic Name	Endovascular Graft
Device Trade Name	EXCLUDER™ Bifurcated Endoprosthesis (See Pages 11-12 for model numbers)
Applicant's Name and Address	W. L. Gore & Associates, Inc. 1327 Orleans Drive Sunnyvale, CA 94089
PMA Application Number	P020004

2.0 Indications and Usage

2.1 Trunk-Ipsilateral Leg Endoprosthesis and Contralateral Leg Endoprosthesis Components

The EXCLUDER Bifurcated Endoprosthesis is intended to exclude the aneurysm from the blood circulation in patients diagnosed with infrarenal abdominal aortic aneurysms (AAA) disease and who have appropriate anatomy as described below:

- Adequate iliac/femoral access
- Infrarenal aortic neck treatment diameter range of 19-26 mm and a minimum aortic neck length of 15 mm.
- Proximal aortic neck angulation = 60°.
- Iliac artery treatment diameter range of 8-13.5 mm and iliac distal vessel seal zone length of at least 10 mm.

2.2 Aortic Extender Endoprosthesis and Iliac Extender Endoprosthesis Components

The EXCLUDER Extender Endoprostheses (Aortic and Iliac) are intended to be used after deployment of the EXCLUDER Bifurcated Endoprosthesis. These extensions are intended to be used when additional length and/or sealing for aneurysmal exclusion is desired.

3.0 Contraindications

There are no known contraindications for these devices.

4.0 Warnings and Precautions

See Warnings and Precautions in the labeling (Instructions for Use)

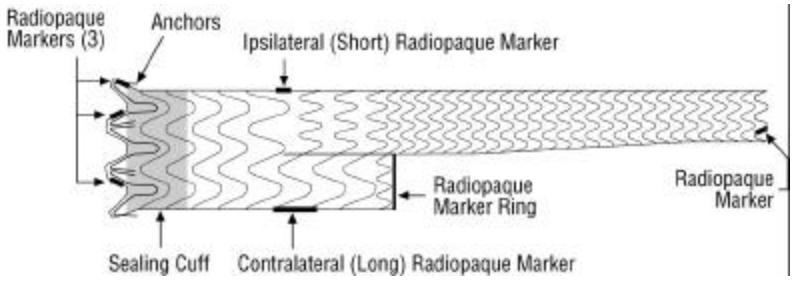
5.0 Device Description

5.1 Trunk-Ipsilateral Leg Endoprosthesis and Contralateral Leg Endoprosthesis Components

The EXCLUDER Bifurcated Endoprosthesis is comprised of two components, the Trunk-Ipsilateral Leg Endoprosthesis (Trunk) (Figure 1) and the Contralateral Leg Endoprosthesis (Figure 2). The graft material is expanded polytetrafluoroethylene and fluorinated ethylene propylene (ePTFE and FEP), and is supported by Nitinol wire along its external surface. Nitinol anchors and an ePTFE/FEP sealing cuff are located at the aortic end of the trunk (Figure 1). An ePTFE/FEP sleeve is used to constrain the endoprostheses on the leading end of the delivery catheters.

Deployment of both endoprosthesis components initiates from the leading (aortic) end and proceeds toward the trailing (iliac) end of the delivery catheter (Figures 3A, 3B, and 3C). The ePTFE/FEP sleeve remains in situ between the endoprosthesis and the vessel wall.

Figure 1: Trunk-Ipsilateral Leg Endoprosthesis



Trunk-Ipsilateral Leg Endoprosthesis Radiopaque Markers

- Three (3) short markers at the aortic end.
- One (1) long and one (1) short marker at the endoprosthesis bifurcation level. The long marker denotes the contralateral leg side location and orientation.
- One (1) marker ring at the opening of the contralateral leg hole.
- One (1) short marker at the iliac end of the ipsilateral leg.

Figure 2: Contralateral Leg Endoprosthesis

Contralateral Leg Endoprosthesis Radiopaque Markers

- One (1) marker at each end

Figure 3A: EXCLUDER Bifurcated Endoprosthesis Delivery Catheter

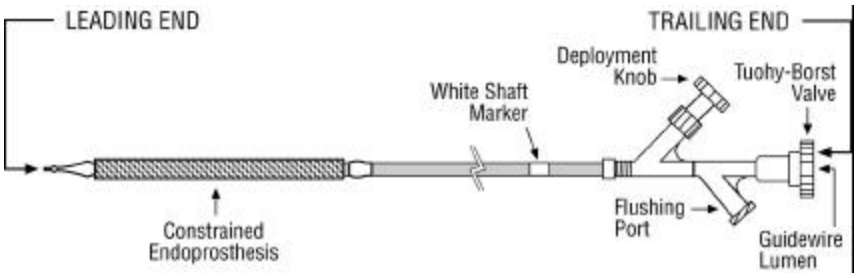


Figure 3B: Constrained EXCLUDER Bifurcated Endoprosthesis (Trunk-Ipsilateral) on Delivery Catheter with Radiopaque Markers

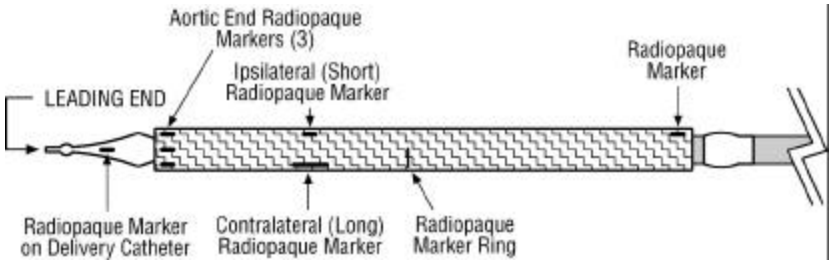
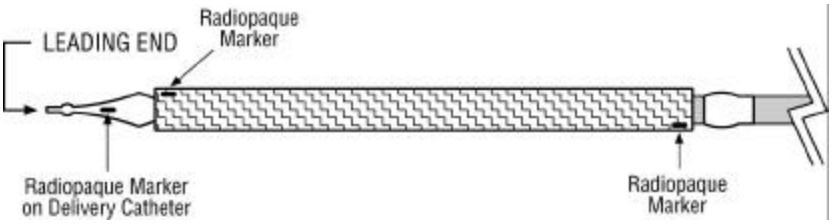


Figure 3C: Constrained EXCLUDER Bifurcated Endoprosthesis (Contralateral) on Delivery Catheter with Radiopaque Markers

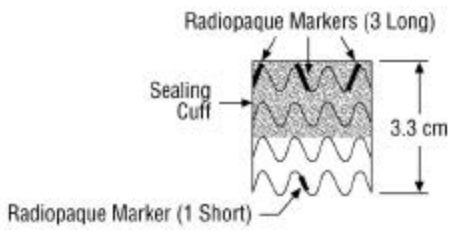


5.2 Aortic Extender Endoprosthesis and Iliac Extender Endoprosthesis Components

5.2.1 Aortic Extender Endoprosthesis

The Aortic Extender Endoprosthesis (Aortic Extender) provides an extension of approximately 1.6 cm of the leading (proximal) end of the Trunk-Ipsilateral Leg Endoprosthesis (Trunk). This extension also allows a minimum of approximately 1.6 cm overlap with the Trunk, and can be overlapped with the Trunk at increasing length, until completely seated within the Trunk if necessary. This allows for customization of extender length based on patient anatomy and physician preference. The graft material is expanded polytetrafluoroethylene and fluorinated ethylene propylene (ePTFE and FEP), and is supported by Nitinol wire along its external surface. An ePTFE/FEP sealing cuff is located near the proximal end of the endoprosthesis (Figure 4). An ePTFE/FEP sleeve is used to constrain the endoprosthesis on the leading end of the delivery catheter (Figures 5A and 5B). Deployment of the Aortic Extender initiates from the trailing (trunk) end and proceeds toward the leading (aortic) end of the endoprosthesis and delivery catheter. Following deployment, the ePTFE/FEP sleeve remains in situ between the endoprosthesis and the vessel wall.

Figure 4: Aortic Extender Endoprosthesis*



Aortic Extender Radiopaque Markers (4 total)

- Three (3) long markers at the proximal or top end
- One (1) short marker at the distal or bottom end

* Note: All dimensions are nominal.

Figure 5A: EXCLUDER Extender Endoprosthesis Delivery Catheter

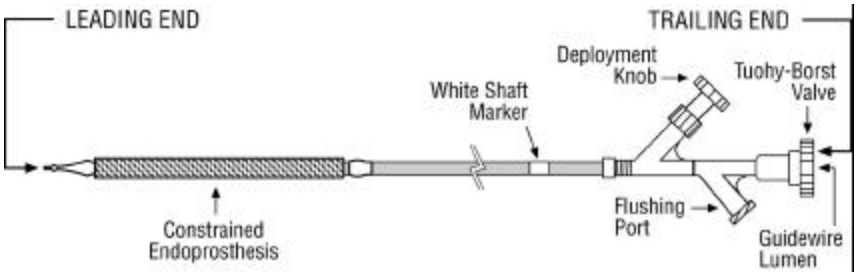


Figure 5B: Constrained EXCLUDER Extender Endoprosthesis (Aortic Extender)

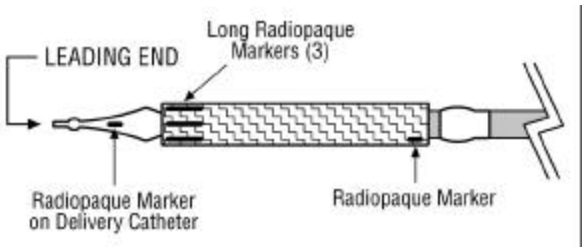
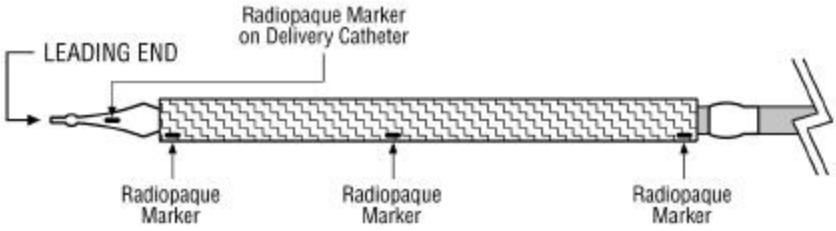


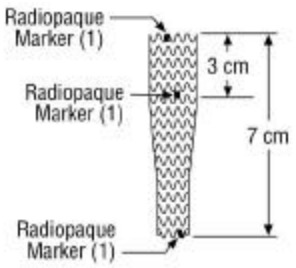
Figure 5C: Constrained EXCLUDER Extender Endoprosthesis (Iliac Extender)



5.2.2 Iliac Extender Endoprosthesis

The Iliac Extender Endoprosthesis (Iliac Extender) provides an extension of up to 4 cm of either the ipsilateral or contralateral limb. The extender component can be placed at variable extension lengths from 4 cm to 0 cm for a complete overlap within the iliac leg component allowing customization of extender treatment length based on patient anatomy and physician preference. The graft material is ePTFE/FEP, and is supported by Nitinol wire along its external surface. A radiopaque marker is located 3 cm from the proximal or top end (Figures 5C and 6). This marker denotes the recommended minimum overlap with the ipsilateral or contralateral limb of the EXCLUDER Bifurcated Endoprosthesis. An ePTFE/FEP sleeve is used to constrain the endoprosthesis on the leading end of the delivery catheter (Figures 5A and 5C). Deployment of the Iliac Extender initiates from the leading (aortic) end and proceeds toward the trailing (iliac) end of the delivery catheter. Following deployment, the ePTFE/FEP sleeve remains in situ between the endoprosthesis and the vessel wall.

Figure 6: Iliac Extender Endoprosthesis*



Iliac Extender Radiopaque Markers (3 total)

- Two (2) end markers: One (1) at each end
- One (1) marker located 3 cm below the proximal end

* Note: All dimensions are nominal.

Table 5.1 Trunk-Ipsilateral Leg Endoprosthesis Sizes

Part Number	Endoprosthesis Aortic Diameter [mm]	Endoprosthesis Iliac Diameter [mm]	Endoprosthesis Length [cm]
PCT231216	23	12	16
PCT231218	23	12	18
PCT231416	23	14.5	16
PCT231418	23	14.5	18
PCT261216	26	12	16
PCT261218	26	12	18
PCT261416	26	14.5	16
PCT261418	26	14.5	18
PCT281216	28.5	12	16
PCT281218	28.5	12	18
PCT281416	28.5	14.5	16
PCT281418	28.5	14.5	18

Table 5.2 Contralateral Leg Endoprosthesis Sizes

Part Number	Endoprosthesis Proximal Diameter [mm]	Endoprosthesis Iliac Diameter [mm]	Endoprosthesis Length [cm]
PCC121000	16	12	10
PCC121200	16	12	12
PCC121400	16	12	14
PCC141000	16	14.5	10
PCC141200	16	14.5	12
PCC141400	16	14.5	14

Table 5.3 Aortic Extender Endoprosthesis Sizes

Part Number	Endoprosthesis Diameter [mm]	Endoprosthesis Lengths [cm]
PCA230300	23	3.3
PCA260300	26	3.3
PCA280300	28.5	3.3

Table 5.4 Iliac Extender Endoprosthesis Sizes

Part Numbers	Endoprosthesis Proximal Diameter [mm]	Endoprosthesis Iliac Diameter [mm]	Endoprosthesis Length [cm]
PCL161007	16	10	7
PCL161207	16	12	7
PCL161407	16	14.5	7

6.0 Alternative Practices and Procedures

The generally accepted treatment for AAA repairs is surgical repair, which involves dissecting the aneurysm and placing a synthetic graft inside the diseased tissue. AAA diagnosed patients who are considered good or acceptable surgical and anesthetic risk are recommended for elective surgical repair when the aneurysm shows rapid growth, becomes symptomatic, or reaches a maximum diameter generally greater than 4.5 cm.
AAA diagnosed patients who are considered unacceptable surgical or anesthesia risk candidates may be medically managed and closely monitored, or recommended for endovascular repair.

7.0 Marketing History

The EXCLUDER Bifurcated Endoprosthesis has been commercially available throughout the world, including Europe, Asia, Latin America and Australia since 1998. The EXCLUDER Bifurcated Endoprosthesis has not been withdrawn from marketing in any country for any reason, including safety or effectiveness.

8.0 Adverse Events

8.1 Observed Adverse Events

A US multi-center, prospective study conducted at 19 centers which included 235 test subjects and 99 control subjects provide the basis of the observed adverse event rates presented in Table 8.1.

Table 8.1 Major Adverse Events

Major Adverse Events	Early (= 30 days)				Late(> 30 days to 12 months)			
	EXCLUDER Bifurcated Endoprosthesis 235	(%)	Control 99	(%)	EXCLUDER Bifurcated Endoprosthesis 231	(%)	Control 97	(%)
Deaths	3	1%	0	0%	14	6%	5	5%
Other Adverse Events								
Aneurysm Size Increase with an Intervention	0	0%	N/A	N/A	1	0.4%	N/A	N/A
Bleeding[1,2]	10	4%	32	32%	1	0.4%	1	1%
Bowel[1]	5	2%	16	16%	6	3%	3	3%
Cardiac[1]	7	3%	14	14%	16	7%	13	13%
Endoleak with an Intervention	0	0%	N/A	N/A	13	6%	N/A	N/A
Genitourinary	1	0.4%	1	1%	6	3%	1	1%
Neoplasm	1	0.4%	0	0%	3	1%	1	1%
Neurologic	1	0.4%	2	2%	7	3%	1	1%
Pulmonary[1]	3	1%	12	12%	10	4%	4	4%
Renal	2	1%	3	3%	5	2%	0	0%
Vascular[1]	3	1%	6	6%	7	3%	5	5%
Wound	7	3%	4	4%	9	4%	2	2%
Other Complications	0	0%	2	2%	12[3]	5%	4	4%

Major Adverse Events from Clinical Study

1 Differences between groups are significantly different for Early Adverse Events (= 30 days).

2 The major adverse event Bleeding threshold for both EXCLUDER Bifurcated Endoprosthesis and control patients is defined as procedural blood loss
> 1000 cc requiring intervention.

3 "Other Complications" in the EXCLUDER Bifurcated Endoprosthesis group were identified by physicians as follows:

1. Reaction to chemotherapy
2. Right axillary hematoma - post transaxillary arteriogram
3. Self inflicted gunshot wound to the head
4. Cholelithiasis with recurrent pancreatitis
5. Recurrent macular pucker, left eye

6. Fractured left humerus with hospitalization
7. Fractured left wrist, injured shoulder and right wrist (fall in hospital while there for ascites)
8. Thrombosis of known popliteal aneurysm
9. Fractured right femur
10. Bilateral carotid stenosis
11. Gynecomastia
12. Cataract and macular pucker, right eye

8.2 Potential Device or Procedure Related Adverse Events

Adverse events that may occur and/or require intervention include, but are not limited to:

- amputation
- aneurysm enlargement
- aneurysm rupture and death
- arterial or venous thrombosis and/or pseudoaneurysm
- arteriovenous fistula
- bleeding, hematoma, or coagulopathy
- bowel (e.g., ileus, transient ischemia, infarction, necrosis)
- cardiac (e.g., arrhythmia, myocardial infarction, congestive heart failure, hypotension or hypertension)
- claudication (e.g., buttock, lower limb)
- death
- edema
- embolization (micro and macro) with transient or permanent ischemia
- endoleak
- endoprosthesis: improper component placement; incomplete component deployment; component migration; separation of graft material from stent; occlusion; infection; stent fracture; graft material failure, dilatation, erosion, puncture, perigraft flow
- fever and localized inflammation
- genitourinary (e.g., ischemia, erosion, fistula, incontinence, hematuria, infection)
- hepatic failure
- impotence
- infection (e.g., aneurysm, device or access sites)
- lymph fistula/complications
- neurologic damage, local or systemic (e.g., stroke, paraplegia, paraparesis)
- occlusion of device or native vessel
- pulmonary complications (e.g., pneumonia, respiratory failure)
- renal (e.g., artery occlusion, contrast toxicity, insufficiency, failure)
- surgical conversion
- wound (e.g., infection, dehisence)
- vascular spasm or vascular trauma (e.g., ilio-femoral vessel dissection, bleeding, rupture, death)

9.0 Summary of Pre-clinical Results

9.1 Biocompatibility

Toxicology and biocompatibility testing was conducted for materials in the EXCLUDER Bifurcated Endoprosthesis System. Testing was conducted in accordance with Federal Good Laboratory Practices per 21 CFR §58. The EXCLUDER Bifurcated Endoprosthesis was classified per ISO 10993 as an implant device with permanent contact. The EXCLUDER Bifurcated Endoprosthesis delivery catheter was classified as an externally communicating device with limited exposure (≤ 24 hr).

Table 9.1 summaries the biocompatibility test results for the implant. Table 9.2 summarizes the biocompatibility test results for the catheter.

Table 9.1 Summary of Biocompatibility Test Results for the Implant

Test Name	Test Method	Results
Cytotoxicity	MEM Elution Test – ISO	Non-Cytotoxic
Sensitization	Kligman Maximization Study – ISO	Non-Sensitizing
Irritation/Intracutaneous Toxicity	Intracutaneous Injection Test - ISO	Negligible Irritant
Acute Systemic Toxicity	Systemic Injection Test - ISO	No significantly greater biological reaction than the controls.
Pyrogenicity	Rabbit Pyrogen Test (Material Mediated) -ISO	Non-Pyrogenic
Hemocompatibility	Hemolysis: Direct Contact-Rabbit Blood – ISO	Non-Hemolytic
Subchronic Toxicity	Canine Implant Study	No Systemic Effects Observed
Genotoxicity/Mutagenicity	*Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay –ISO	Non-Mutagenic
	CHO/HGPRT Forward Mutation Assay –ISO	Non-Mutagenic
	Chromosomal Aberration Assay –ISO	Non-Clastogenic
Implantation	Intramuscular Implantation –ISO	Test Article and Negative Control had Comparative Results
Chronic Toxicity	Canine Implant Study	No Systemic Effects Observed

Table 9.2 Summary of Biocompatibility Test Results for the Catheter

Test Name	Test Method	Results
Cytotoxicity	MEM Elution Test – ISO	Non-Cytotoxic
Sensitization	Kligman Maximization Study – ISO	Non-Sensitizing
Irritation/Intracutaneous Toxicity	Intracutaneous Injection – ISO	Negligible Irritant
Acute Systemic Toxicity	Systemic Injection Test – ISO	Non-Toxic
Pyrogenicity Test	Rabbit Pyrogen Test (Material Mediated) – ISO	Non-Pyrogenic
Hemocompatibility	Hemolysis Rabbit Blood – ISO	Non-Hemolytic

All test results indicate that the materials and processes used to manufacture the EXCLUDER implant and catheter are biocompatible and suitable for their intended use.

9.2 Product Testing

W. L. Gore and Associates, Inc. (GORE), conducted comprehensive pre-clinical bench and analytical testing on the EXCLUDER Bifurcated Endoprosthesis (EBE) implant and delivery system. The express intent of this *in vitro* testing was to verify that the performance attributes of the EBE system are sufficient to minimize the risk of adverse events under anticipated clinical use conditions. Results obtained from the *in vitro* test regimen provide evidence substantiating the safety and effectiveness of the EBE system.

A summary of results is presented below for each of the *in vitro* tests. Table 9.4 summarizes test results associated with the functional requirements of the delivery system, and Table 9.5 summarizes test results related functional requirements of the implant.

The results of the *in vitro* testing, taken as a whole, demonstrate that the EBE system meets established functional requirements for aortic endovascular devices. Furthermore, these data substantiate the safety and effectiveness of the EBE system, which, consequently, is expected to perform as intended when used in accordance with its labeled indications.

9.2.1 Delivery System Test Results Summary

The following table contains test results that were performed to evaluate the ability of the EBE delivery system to access the implant location, accurately deploy the device, safely withdraw the delivery system catheter, maintain hemostasis, and be fluoroscopically visualized.

Table 9.3 Summary of Test Results Related to the EBE Delivery System Functionality

In Vitro Test	Relevant Functional Requirement	Summary of Test Results
Catheter Angular Rotation to Failure Test	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system	Twenty sterilized, finished delivery systems with mounted devices were tested in a 37° C water bath to determine angular rotation to failure. All delivery systems were tested in both clockwise and counter-clockwise rotation of 360° and then to failure noting the failure angle and failure. Based on the results of these tests, the EBE delivery catheters would not be expected to fail in torsion during anticipated clinical use.
Catheter Bond Tensile Strength Test	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system	The longitudinal tensile strength of the critical bonds and joints of the EBE delivery catheters were determined. A total of 158 catheter bonds were tested. Results indicate that there is at least 95% confidence level that the minimum tensile strength of each critical catheter junction will exceed the ISO 10555-1 standard of 3.37lbf.
Catheter Deployment Knob-Line Assembly Tensile Test	• Ability to deploy the implant	The tensile strength of the catheter deployment knob/line assembly (n=60) was determined to demonstrate conformance to design requirements. Mean deployment knob/line assembly strength was 4.06 lbf. The data demonstrates that there is at least 95% confidence that there is a 95% probability that any individual deployment knob/line tensile strength exceeds the maximum expected deployment force.
Catheter Leak Test	• Hemostasis of the delivery system	The leak resistance of the delivery catheters was evaluated. No catheter leakage was observed in any of the test samples when tested up to pressures of 20 atmospheres. These data indicate there is a 95% confidence that there is at least a 95% probability that any EBE delivery catheter will meet the minimum design requirement of 1.5 atm.
Catheter Length Test	• Ability to access the intended location • Ability to deploy the implant	The minimum and maximum expected catheter working lengths for 60 delivery system configurations tested met the established design specifications at a minimum confidence level of 95%.
Catheter Profile Test	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system • Hemostasis of the delivery system	A total of 114 measurements were made on a total of 90 final sterilized delivery catheters. All tested catheter shafts met the design specifications (0.130mm ± 0.002mm) with at least 95% confidence. Compatibility with recommended introducer sheath accessories is expected.
Catheter Torsional Bond Strength Test	• Ability to access the intended location • Ability to deploy the implant	The torsional strength of the two catheter junctions that will be subjected to the greatest torsional load during deployment were determined to have torsional bond strengths significantly in excess of established

***In Vitro* Test**	**Relevant Functional Requirement**	**Summary of Test Results**
	• Ability to withdraw the delivery system	design specifications. The results show that the catheter junctions can withstand up to 160 inches – ounces of torque without any failures, to a confidence/reliability level of 95%/95%.
Delivery System Accessory Compatibility	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system • Hemostasis of the delivery system	A total of 60 sterilized, finished devices were tested for dimensional compatibility; all tested samples successfully passed the guidewire through the lumen and were able to be passed through the appropriately sized sheath. All delivery system configurations were dimensionally compatible with the recommended guidewires and 12F and 18F introducer sheaths per established design specifications.
Delivery System Deployment Force Test	• Ability to deploy the implant	The force required to deploy the EBE was determined. The mean peak deployment force of the Trunk-Ipsilateral Leg component was 1.70lbf; the mean peak deployment force of the Contralateral Leg component was 1.23 lbf. Using the Trunk-Ipsilateral Leg as a conservative measure of expected deployment force, the one sided upper bound from the prediction interval for individual peak deployment force is 2.11 lbf. The maximum expected deployment force does not exceed the minimum expected strength of the EBE delivery catheter deployment knob/line tensile strength.
Delivery System Deployment Reliability Test	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system	A comprehensive evaluation of *in vitro* deployments was conducted in a clinically relevant model at 37° C. A total of 284 finished sterilized devices including appropriate introducer sheaths, guidewires, and balloon catheters were used and were tested with 100% deployment success. Binomial statistics demonstrate with a 95% confidence level that at least 98% of the EBE will access the intended implant location, safety deploy the implant, and be successfully withdrawn when used in a manner consistent with labeling or under anticipated clinical use.
Delivery System Radiopacity Confirmation Test	• Fluoroscopic visualization	Tissue density was simulated by aluminum plates of varying densities: 1.0 cm, 2.0 cm, and 3.0 cm. An Integris V-3000 (Phillips Imaging, Inc.) digital fluoroscope was used for imaging. The results of the *in vitro* radiopacity testing show that the radiopacity of the EBE delivery systems have sufficient radiopacity for clinical use.
Delivery System Torquability Test	• Ability to access the intended location • Ability to deploy the implant	The torque response of the delivery system and the torque effect on deployment reliability were evaluated. All 130 tested delivery systems exhibited acceptable torque response after being tracked through an *in vitro* aneurysmal deployment model.

***In Vitro* Test**	**Relevant Functional Requirement**	**Summary of Test Results**
	• Ability to withdraw the delivery system	Acceptable torque response was defined as 360° rotation clockwise and counterclockwise from the neutral position in the Trunk-Ipsilateral Leg component and, for the Contralateral Leg component and extenders, distal tip rotation of at least 90°. All tested delivery systems deployed successfully after being subjected to design-specific torque testing.
Sewn Sleeve (Corset) Burst Strength Test	• Ability to access the intended location • Ability to deploy the implant	The burst strength of representative corsets was characterized (150 – 593 psi) and determined to be adequate to constrain the stent-graft prior to implantation.

9.2.2 Implant Test Results Summary

The following table contains tests results that were performed to assess the EBE implant's ability to accurately deploy, fixation effectiveness, durability, ability to exclude the aneurysm (permeability considerations), modularity, sizing, patency, and MRI compatibility, and ability to be fluoroscopically visualized.

Table 9.4 Summary of Test Results Related to the EBE Implant Functionality

***In Vitro* Test**	**Relevant Functional Requirement**	**Summary of Test Result**
Acute Anchoring Test	• Fixation effectiveness of the implant	Acute resistance to migration of the EBE was demonstrated under simulated physiological conditions when used in a manner consistent with those set forth in the Instructions for Use (over-sizing, appropriate device placement, post-deployment balloon touch-up). For this test, maximum allowable device displacement after deployment was defined as ± 1 mm. A total of 100 final sterilized EBE components were tested with no observed acute migration after exposure to simulated flow conditions.
Accelerated Anchor Fatigue Test	• Durability and integrity of the implanted device	Anchor fatigue resistance was evaluated for 10 years simulated physiological loading (380 million cycles) under "worst-case" test conditions. Samples were subjected to severe loading, far in excess of clinically expected loads. Only one anchor fatigue fracture out of 112 tested anchors was noted at the ten-year equivalent inspection. The fractured anchor was attached to the stent-graft. No compromise of device function was noted. From the data generated from this "worst-case" testing, it is expected that the anchors will survive ten years of pulsatile loading under anticipated physiological conditions without fatigue related anchor fracture or compromise of device fixation.
Deployment Accuracy Test	• Ability to accurately deploy	The Aortic Extender was selected for deployment testing as it is the component most likely to produce deployment inaccuracies. Based on testing in straight and angulated segments of an *in vitro* test model, the EBE is expected to be deployed no more than 5 mm proximal to the intended implant site at a 95% confidence level. Testing was performed on 39 final sterilized Aortic extenders using a physiological pulsatile pressure and flow model maintained at 37° C. All samples met the acceptance criteria of deployment within 5 mm proximal of the intended location.
Endoprosthesis Radiopacity Confirmation Test	• Fluoroscopic visualization	The radiographic visibility of the EBE was determined to be sufficient for clinical use when compared to clinically validated devices under a range of simulated tissue densifications. Tissue density was simulated by aluminum plates of varying densities: 1.0 cm, 2.0 cm,

In Vitro Test	Relevant Functional Requirement	Summary of Test Result
		and 3.0 cm. An Integris V-3000 (Phillips Imaging, Inc.) digital fluoroscope was used for imaging. The results of the *in vitro* radiopacity testing show that the radiopacity of the EBE delivery systems have sufficient radiopacity for clinical use.
Finite Element Analysis	• Durability and integrity of the implanted device	The location and magnitude of the maximum strains in the EBE Nitinol wire frame were analytically determined as a function of radial compression when subjected to catheter loading and an *in vivo* pulsatile loading environment. Peak strain magnitudes at simulated catheter loading are predicted to be below the ultimate tensile strain of the Nitinol wire. Maximum strain locations and values determined from the simulated *in vivo* pulsatile loading were subsequently used as a reference in appropriate *in vitro* testing including pulsatile fatigue testing and wear and migration testing.
Integral Water Permeability	• Fixation effectiveness of the implant • Permeability considerations • Testing of the modularity of the endovascular system	The integral water permeability of the EBE modular components was determined. Integral Water Permeability of all EBE components was calculated and shown to be between 0.05 and 1.57 ml/min/cm^2 using methods defined in AMSI/AAMI VP20 – 1994. The integral water permeability observed in the 129 EBE devices tested is less than the water permeability of polyester materials used in endovascular and vascular applications.
Longitudinal Tensile Strength Test	• Durability and integrity of the implanted device	The longitudinal tensile strength of 44 final sterilized EBE devices was characterized and compared to the appropriate ePTFE graft design specifications using the methods as defined in ANSI/AAMI VP20 - 1994. All tensile strengths exceed the established specifications of 4.14 kg.
Magnetic Resonance Imaging Safety Test	• MRI compatibility	The EBE is not expected to present an additional hazard or risk when implanted in a patient subjected to MRI at 1.5-Tesla. There were no observable magnetic field interactions, minimal MRI-related heating (<1.0°C), and only minor image artifacts. The device has therefore been determined to be MRI safe under these conditions.
Microscopic Determination of Porosity Test	• Permeability considerations • Patency of the implant	The fibril length of the ePTFE material comprising the luminal surface of the EBE was determined using methods defined in ANSI/AAMI VP20 - 1994. The data from 25 final sterilized EBE devices (10 measurements in 3 regions per sample) ranged from 20.0 - 26.2 µm. The fibril length of the EBE luminal surface is consistent with that of GORE-TEX® Vascular Grafts successfully used in aortic applications.

***In Vitro* Test**	**Relevant Functional Requirement**	**Summary of Test Result**
Nitinol Material Analysis Test	• Durability and integrity of the implanted device	The bulk material and surface of the Nitinol wire used for the EBE were chemically analyzed and quantified, indicating 55 weight percent nickel and 44.5 weight percent titanium, with trace amounts of carbon, oxygen, and hydrogen. The surfaces of the wire were also examined under SEM to detect defects and contamination. The bulk material analysis and surface analysis met design requirements. Surface observations with SEM demonstrated a consistently smooth wire surface with no unacceptable anomalies such as pitting, cracks, or contaminants.
Nitinol Stent Corrosion Resistance Test	• Durability and integrity of the implanted device	The corrosion resistance of both the Nitinol wire and the complete EBE was analyzed using potentiodynamic polarization testing in a simulated *in-vitro* environment (Hanks Balanced Salt Solution pH 7.4 at 37° C). The results of the potentiodynamic polarization tests showed that the average corrosion rate predicted for the base Nitinol wire stent is 343×10^{-6} mm/yr, whereas the EBE device is 10 fold less, or 34×10^{-6} mm/yr. The finished EBE device has an average predicted corrosion rate less than 316L stainless steel under the test conditions.
Nitinol Thermo-mechanical Properties Test	• Durability and integrity of the implanted device.	The thermodynamic and mechanical attributes of the Nitinol wire used in the EBE were assessed for conformance with established design specifications. All test articles had an austenitic finish temperatures (A_f) below 35°C, and therefore met the established design specifications. Tensile testing was performed on samples of all wire sizes to characterize the mechanical properties of the material. These properties include tensile strength, mean elongation at break, ultimate tensile loading plateau, and tensile permanent set after deformation. The results demonstrate that the mechanical properties of the processed wire meet or exceed, as appropriate, the established acceptance criteria. Samples of the three diameters of Nitinol wire utilized in device manufactured on tensile testing recorded the following material characteristics: ulitmate tensile strength (range 1471 – 1512 MPa), mean elongation at break (range 11.2 – 12.4 %), mean tensile loading plateau (range 535 – 561 MPa), and mean tensile permanent set (0.04 – 0.15%) after initial deformation.
Pull Test for Modular Components	• Testing of the modularity of the endovascular system	The force required to separate the modular components of the EBE in an *in vitro* setting was determined using an Instron mechanical tester at 37° C. Mean peak force to pull the Contralateral Leg from the Trunk Ipsilateral Leg ranged from 0.909 lbf to 1.478 lbf. based on 3cm overlap as described in the IFU. The average

***In Vitro* Test**	**Relevant Functional Requirement**	**Summary of Test Result**
		longitudinal separation (pull-out) forces are expected to be sufficient for clinical use.
Pulsatile Fatigue Test	• Durability and integrity of the implanted device	After 10 years simulated physiological loading of 380 million cycles, tested samples were examined visually and with magnification (30x and SEM). There was no evidence of Nitinol wire pitting or cracking, nor of fatigue related fractures. No wear, abrasion, or migration between the overlapping portion of the trunk-ipsilateral leg and contralateral leg were noted. The device was intact after 10 years simulated *in vivo* physiological loading of 380 million cycles with no perforation or detachment of the ePTFE graft as a result of pulsatile fatigue testing.
Radial Compression Strength Test	• Fixation effectiveness of the implant • Appropriate Sizing of the implant • Patency of the implant	The radial compression forces of the EBE components were characterized at the appropriate diameters representative of clinically relevant oversizing. Load data were collected for the 23mm Trunk component, 26mm Trunk component, 28.5mm Trunk component, 12mm Contralateral Leg, 14.5mm Contralateral Leg, the 23mm, 26mm and 28.5mm Aortic Extender, and the 10mm Iliac Extender at both 10 and 20 % oversizing. Load data were collected using a 1cm wide ribbon and are representative of the force to uniformly compress 1cm of device length. Radial compression strength ranged from a mean of 0.212 lbf – 0.754 lbf. The radial compression strengths of the EBE are anticipated to be adequate for clinical use.
Sealing Test	• Fixation effectiveness of the implant • Permeability considerations • Testing of the modularity of the endovascular system	The overall rate of fluid loss around and through the various modular components of the EBE when deployed in a flow model was characterized in 55 sterilized final devices. The total rate of fluid loss for the worst case EBE configurations, inclusive of the leakage at the modular junctions and the permeability of the graft material, was 234-366 ml/min, approximately the permeability of commercially available polyester materials used in vascular and endovascular applications, which range from 310-800 ml/min.
Stent-Graft Bend Radius Test	• Ability to accurately deploy • Fixation effectiveness of the implant • Patency of the implant	The bend radii (without kinking) of the various components of EBE were characterized using 71 final sterilized devices. Mean bend radii range from 0.39 inches to 1.00 inches, depending on component tested. Comparison to published literature shows that the EBE System is capable of accommodating typical aorto-iliac anatomy without kinking.

***In Vitro* Test**	**Relevant Functional Requirement**	**Summary of Test Result**
Stent-Graft Burst Strength Test	• Durability and integrity of the implanted device	The burst strength of the EBE components was determined and compared to the appropriate ePTFE graft design specifications per ANSI/AAMI VP:20 – 1994. Mean burst strength ranged from 76.4 psi – 126.4 psi on the 43 components tested (trunk, leg or extender). All burst strengths exceeded the minimum design requirements.
Stent-Graft Diameter and Wall Thickness Test	• Testing of the modularity of the endovascular system • Appropriate sizing of the implant	The outer diameters and wall thickness of the deployed EBE components were characterized and verified in accord with ANSI/AAMI VP:20 – 94. The outer diameter and wall thickness of 120 final sterilized EBE devices were tested. All components tested met the appropriate design requirements of 0.002 – 0.012 inches diameter, and stent graft outer diameter of 10.0 – 29.7mm, depending on component size.
Stent-Graft Length Test	• Ability to accurately deploy • Appropriate sizing of the implant	The length of the 90 EBE components, mounted on the delivery catheters was measured and compared to relevant design specifications in a manner consistent with ANSI/AAMI VP:20-94. Acceptance criteria range from ± 0.3cm - ± 0.6cm from the nominal length. All devices tested met the acceptance criteria.
Stent-Graft Profile Test	• Appropriate sizing of the implant	The profiles of 80 final sterilized EBE devices mounted on delivery catheters were assessed to assure dimensional compatibility with recommended introducer sheath sizes per ISO/CD 15539-1 (Draft 2000). All devices were successfully passed through the appropriate hole gauge.
Wear and Migration Test	• Fixation effectiveness of the implant • Durability and integrity of the implant • Testing of the modularity of the endovascular system	Endoprosthesis integrity was intact after 5 and 10 years simulated physiological loading of 190 million and 380 million cycles, respectively. Test conditions included simulated compliance of 4-7% with pulsatile pressures cycle between approximately 90mm Hg and 130mm Hg. Although test specimens showed artifactual evidence of extensive pulsatile testing, no modular component migration or wire fatigue fracture was noted. Neither significant detachment of the stent-graft, nor wear-induced perforations were noted. There was no obstruction of the graft lumen.

A robust test and analysis regimen was constructed to characterize the mechanical attributes of the EBE. The results of the *in vitro* testing, taken as a whole, demonstrate that the EBE system meets established functional requirements for aortic endovascular devices. Furthermore, these data substantiate the safety and effectiveness of the EBE system by providing evidence that the mechanical attributes of the device have met design goals appropriate for the repair of abdominal aortic aneurysms.

9.3 Animal Studies

Three preclinical *in vivo* studies were conducted to evaluate the performance of the EXCLUDER Bifurcated Endoprosthesis. A canine model was used to assess the ability of the delivery system to successfully access the target site, deploy the graft and be withdrawn from the vasculature, to assess device functionality, and to assess the sub-chronic and chronic biological response to the implanted endoprosthesis. A bovine model, in a near human-size animal, was used for acute assessment of the delivery system to successfully access the target site, deploy the graft and be withdrawn from the vasculature, and the ability of the device to resist migration. An additional bovine model was used to evaluate the deployment system and device functionality of Aortic and Iliac Extender Endoprostheses. A summary of these studies follows in Table 9.5.

Table 9.5 Summary of Preclinical *In Vivo* Studies

Animal Study	#/ Type of Animal	Test Article	Methods	Results/ Conclusions
Sub-chronic and Chronic Study of Bifurcated Endoprosthesis	15 Canines	Scaled-down, trunk-ipsilateral leg, contralateral leg devices, and delivery catheter.	Catheter delivery and device functionality were assessed sub-chronically and chronically in 15 animals. Two sub-chronic animals were maintained in life for approximately one week. Additionally, three canines were maintained in life for one month, one canine for two months, three canines for three months, and four canines for six months. Two canines in the chronic phase were retrieved within one day post-op.	All devices were successfully delivered and deployed. The functional requirements of the device were met and the devices performed as intended. All devices were patent at retrieval, and the host tissue response was judged to be acceptable at both gross and histological examination. There was no evidence of device/component migration or graft disruption.
Acute Study of Bifurcated Endoprosthesis	6 Bovines	Human size, trunk-ipsilateral leg, contralateral leg devices, and delivery catheter.	Six bovines were assessed for acute delivery catheter and device functionality.	All devices were successfully and accurately deployed. The devices were patent and exhibited normal antegrade flow after deployment. There was no evidence of migration or graft disruption.
Acute Study of Aortic and Iliac Extenders	2 Bovines	Human size, aortic and iliac extender devices. Short trunk endoprosthesis and delivery catheter.	Six aortic extenders on long catheters, six iliac extenders on catheters, and six short trunks were deployed in two bovines. These animal procedures were assessed for acute delivery catheter and device performance of the aortic and iliac extender components.	All devices were successfully deployed. Both aortic and iliac extenders could be accurately placed and deployed within another stent-graft or separately. Radiographic evidence showed that no migration had occurred during the acute phase. Post-deployment angiography showed patency.

10.0 Summary of Clinical Studies

10.1 Objectives

The primary objective of the clinical study was to evaluate the safety and effectiveness of the EXCLUDER Bifurcated Endoprosthesis as an alternative to open surgical repair in the primary treatment of infrarenal abdominal aortic aneurysms. Safety was determined by evaluating whether the EXCLUDER Bifurcated Endoprosthesis subjects would have a total proportion of major adverse events that is less than the subjects treated with open surgical repair as evaluated through one year follow-up. Effectiveness was based on exclusion of the aneurysm including the absence of any endoleak, the absence of aneurysm enlargement (= 5 mm), and the absence of major device efficacy adverse events evaluated through one year follow-up. Secondary objectives included an assessment of clinical benefit and quality-of-life measures.

10.2 Study Design

This prospective, non-randomized, multi-center clinical study was designed to compare patients treated with endovascular repair to an open surgical repair control group. Nineteen US sites enrolled 235 EXCLUDER Bifurcated Endoprostheses and 99 control subjects. The control group included patients whose vascular anatomy may not have been suitable for endovascular AAA repair. The ratio of EXCLUDER Bifurcated Endoprostheses to control subjects was approximately 2:1. Follow-up evaluations were scheduled for pre-discharge, 1 month, 6 months, 12 months and annually thereafter. Twelve and 24 month data are provided in this summary based on findings from an independent Core Lab facility. An independent Core Lab facility reviewed CT scans and abdominal X-rays to assess aneurysm diameter changes, device and relative component migration, device integrity (wire and graft) and the presence and type of endoleaks.

Table 10.1 Patient Follow-up and Accountability

Treatment	EXCLUDER Bifurcated Endoprosthesis (N=235)*			Control (N=99)*		
Post-Procedure Interval	1 Month	12 Month	24 Month	1 Month	12 Month	24 Month
Expired	3	14	30	0	5	6
Withdrawn / Lost to Follow-up	0	6	17	2	13	20
Available Subjects	232	215	188	97	81	73
Actual Visit	226	202	177	88	74	67
Site CT Imaging	223	199	168	N/A	68	65
Core Lab CT Imaging	218	196	155	N/A	64	62
Site X-ray Imaging	N/A	163	148	N/A	N/A	N/A
Core Lab X-ray Imaging	N/A	154	129	N/A	N/A	N/A
Site Evaluated for Endoleak	221	199	165	N/A	N/A	N/A
Core Lab Evaluated for Endoleak	180	156	119	N/A	N/A	N/A
Site Evaluated for Aneurysm Enlargement	N/A	191	158	N/A	N/A	N/A
Core Lab Evaluated for Aneurysm Enlargement	N/A	181	146	N/A	N/A	N/A

* Data analysis sample size varies for each of the timepoints above and in the following tables. This variability is due to patients available for follow-up, as well as, quantity and quality of images available from specific timepoints for evaluation. For example, the number and quality of images available for evaluation of endoleak at 12 months is different than the number and quality of images available at 24 months due to variation in the number of image exams performed, the number of images provided from the clinical site to the Core Lab, and/or the number of images with acceptable evaluation quality. Another example is images that may have been interpretable by the Core Lab for flow channel narrowing but the same images may not necessarily have been interpretable for trunk migration.

10.3 Patient Demographics

Tables 10.2 and 10.3 compare the subject characteristics and initial aneurysm diameter of the EXCLUDER Bifurcated Endoprosthesis and open surgical population, respectively.

Table 10.2 Comparison of Subject Characteristics

Characteristic	EXCLUDER Bifurcated Endoprosthesis (N=235)		Control (N=99)		P-Value
	N	(%)	N	(%)	
Average Age (range in years)	73.0	(48-91)	70.01	(51-87)	0.002
Gender: Male Female	204 31	87% 13%	73 26	74% 26%	0.004
Aneurysm Symptomatic	11	5%	15	15%	<0.001
Arrhythmia	56	24%	21	21%	0.591
Bleeding Disorder	11	5%	1	1%	0.119
Cancer	59	25%	19	19%	0.243
Congestive Heart Failure	22	9%	8	8%	0.708
COPD	62	26%	25	25%	0.830
Coronary Artery Disease	145	62%	53	54%	0.165
Erectile Dysfunction (males only)	33	16%	10	14%	0.616
Family History of AAA	14	6%	9	9%	0.307
Hepatic Dysfunction	6	3%	1	1%	0.679
Inflammatory AAA	2	1%	1	1%	1.00
Long-Term Use of Steroids	8	3%	1	1%	0.290
Other Concomitant Aneurysms	18	8%	13	13%	0.116
Peripheral Arterial Occlusive Disease	38	16%	14	14%	0.640
Paraplegia	0	0%	0	0%	N/A
Prior Vascular Intervention	26	11%	10	10%	0.796
Renal Dialysis	0	0%	0	0%	N/A
Smoking History	208	89%	84	85%	0.357
Stroke	26	11%	10	10%	0.818
Thrombotic Event	17	7%	4	4%	0.332
Valvular Heart Disease	18	8%	7	7%	0.852

Table 10.3 Aneurysm Diameter Distribution

Diameter Range	EXCLUDER Bifurcated Endoprosthesis (N=235)		Control (N=99)	
	N	(%)	N	(%)
< 30 mm	0	0%	0	0%
30 - 39 mm	0	0%	0	0%
40 - 49 mm	61	26%	15	15.3%
50 - 59 mm	109	46.4%	46	46.9%
60 - 69 mm	44	18.7%	22	22.2%
70 - 79 mm	15	6.4%	10	10.2%
80 - 89 mm	4	1.7%	5	5.1%
= 90 mm	2	0.9%	1	1.0%

10.4 Results

Data gathered in Tables 10.4 through 10.15 were collected by the clinical study sites and Core Lab. Table 10.4 describes the types of devices implanted into the clinical study patients. Table 10.5 summarizes longer-term device performance compared to control subjects, and Kaplan-Meier data at both 12 and 24 months. Figures 7 through 10 depict Survival at 24 months (Figure 7), Freedom from Aneurysm Related Mortality (Figure 8), Freedom from First Major Adverse Event (Figure 9), and Cumulative Major Adverse Event Rates (Figure 10). Error bars in Figures 7, 8, 9 and 10 represent a 95% confidence limit.

Table 10.4 Devices Implanted

	N	(%)
Number of EXCLUDER Bifurcated Endoprosthesis Subjects	235	100%
Devices Implanted		
Trunk/Ipsilateral Leg and Contralateral Leg[1]	159	67%
with Aortic Extender(s)[2]	17	7%
with Iliac Extender(s)[3]	53	23%
with Aortic and Iliac Extender(s)[4]	6	3%

[1] N = 5 Subjects received one Trunk-Ipsilateral Leg Endoprosthesis and two Contralateral Leg Endoprostheses.

[2] N = 2 Subjects received two Aortic Extender Endoprostheses.

[3] N = 9 Subjects received more than one Iliac Extender Endoprosthesis (2, 3, or 4 Iliac Extenders).

[4] N = 2 Subjects received two Iliac Extender Endoprostheses.

Table 10.5 Summary of Kaplan-Meier Curves to 24 Months

	Total Number of Patients Reaching Follow-up		Aneurysm Rupture		Conversion to Surgical Repair	Death		Aneurysm Related Death[1]		Major Adverse Event	
	T N	C N	T N	C N	T N	T N (%)	C N (%)	T N (%)	C N (%)	T N (%)	C N (%)
Intra-operative	235	99	0	0	0	0	0	0	0	n/a[2]	n/a[2]
≤ 30 Days	235	99	0	0	0	3 1%	0	3 1%	0	32[3] 14%[3]	56[3] 57%[3]
> 30 Days to 12 Months	232	97	0	0	0	11 5%	5 5%	1 0.4%	2 2%	57 27%	24 25%
12 Months to 24 Months	214	82	0	0	0[4]	16 7%	1 1%	0	0	37 17%	10 12%
Total Patients (at 24 Months)	214	82	0	0	0	30	6	4	2	110[5] 47%	65[5] 66%
Kaplan-Meier Summaries			Freedom from Aneurysm Rupture		Freedom from Conversion	Probability of Survival		Freedom from Aneurysm Related Death		Freedom from Major Adverse Event	
12 Month Kaplan-Meier	232	97	100%	100%	100%	94%	95%	98%	98%	65%[3]	36%[3]
24 Month Kaplan-Meier	214	82	100%	100%	100%	87%	93%	98%	98%	52%[3]	33%[3]

T = EXCLUDER Bifurcated Endoprosthesis C = Control

[1] Aneurysm related death is defined as all deaths due to aneurysm rupture, a primary or secondary procedure, surgical conversion, or within 30 days of the primary or secondary procedure. (Chaikof; J Vasc Surg 2002;35:1048-60)

[2] Major adverse events during the intraoperative period are reported in the ≤ 30 day period.

[3] Statistically significant, P < .05

[4] Three elective conversions post 24 months. Three elective conversions occurred > 24 months post-operative. Two conversions were due to aneurysm enlargement and one conversion was due to aneurysm enlargement with a persistent Type II endoleak. All conversions were elective with no ruptures.

[5] Total number of patients with a first adverse event only.

Figure 7: Survival at 24 Months

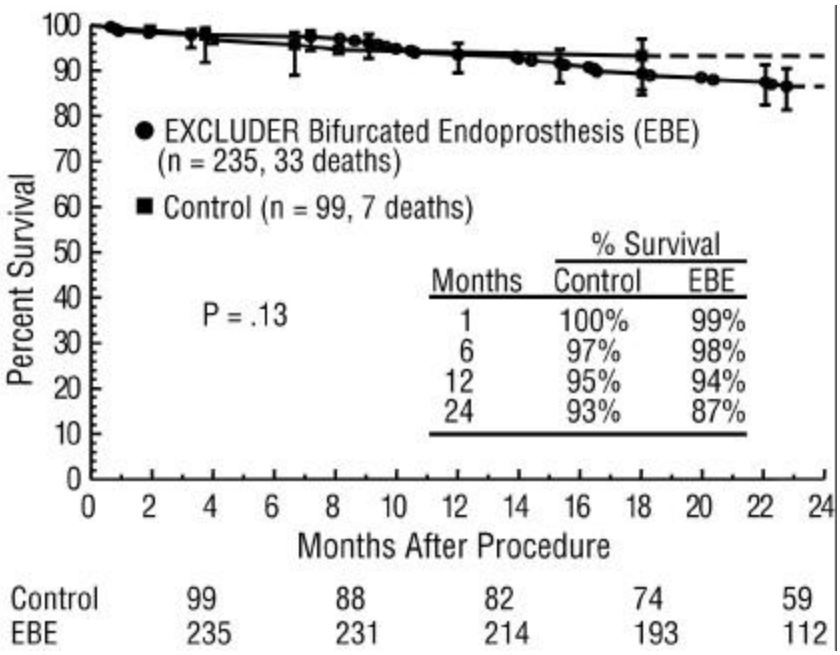


Figure 8: Freedom from Aneurysm Related Mortality

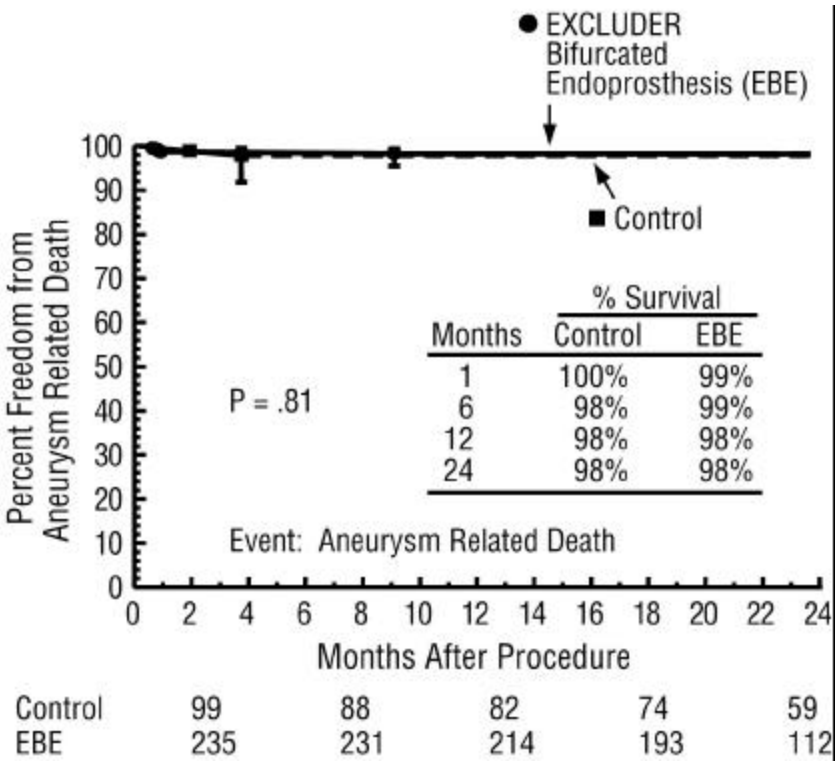


Figure 9: Freedom from First Major Adverse Event

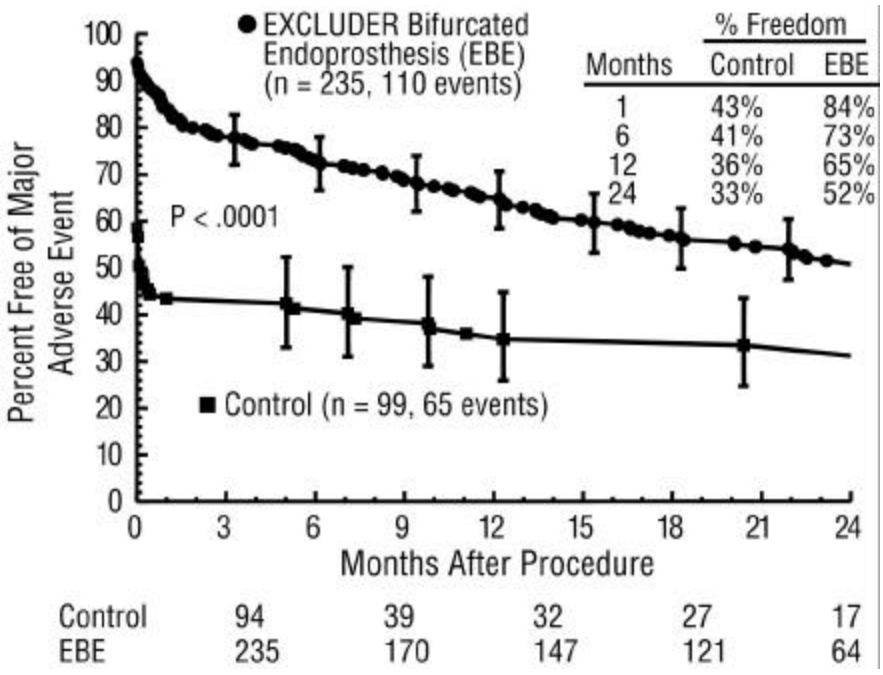
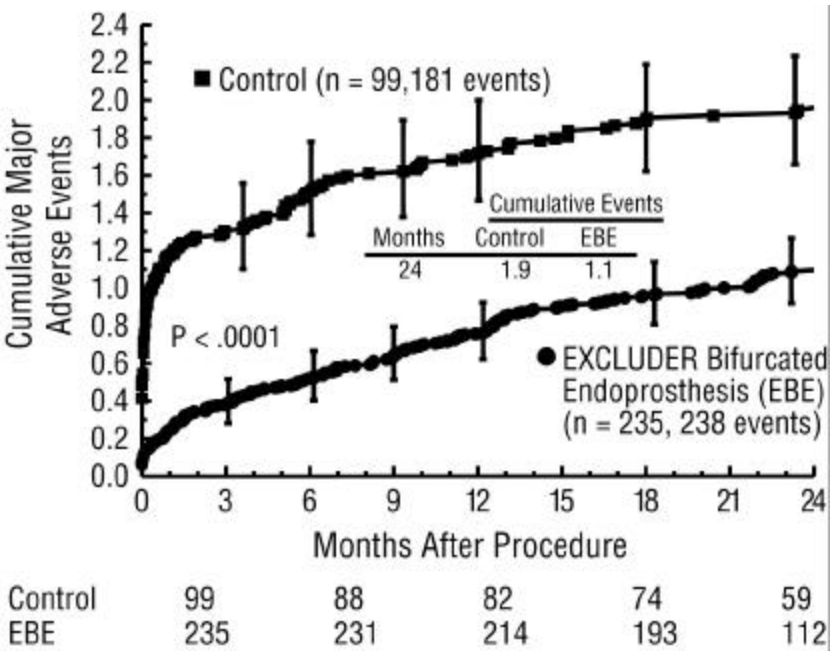


Figure 10: Cumulative Major Adverse Event Rates



Tables 10.6 through 10.13 describe results of the EXCLUDER Bifurcated Endoprosthesis subjects as reported by the Core Lab. Device performance factors analyzed by the Core Lab included device integrity (Table 10.6), device patency (Table 10.7), migration (Tables 10.8 and 10.9), and aneurysm exclusion (Tables 10.10-10.13). Device integrity encompasses the structural findings of the wire-form via abdominal X-ray images at the corresponding follow-up timepoints.

Table 10.6 Abdominal X-ray Findings - Device Integrity*

Device Integrity: Abdominal X-ray	Discharge (N=171)		6 Months (N=156)		12 Months (N=140)		24 Months (N=117)	
	N	(%)	N	(%)	N	(%)	N	(%)
Subjects Free from Device Integrity Issues	170	99%	156	100%	140	100%	117	100%
- Fracture	1	0.6%	0	0%	0	0%	0	0%

* None resulted in clinical sequelae.

Table 10.7 CT Findings – Narrowing of the Flow Channel*

CT - Narrowing	1 Month (N=212)		6 Months (N=193)		12 Months (N=185)		24 Months (N=148)	
	N	(%)	N	(%)	N	(%)	N	(%)
EXCLUDER Endoprosthesis	3	1.5%	0	0%	2	1.1%	2	1.4%

* None affected device patency.

Table 10.8 CT Findings – Trunk Migration*

CT – Trunk Migration	6 Month (N=171)		12 Months (N=175)		24 Months (N=144)	
	N	(%)	N	(%)	N	(%)
Trunk Migration (≥ 10mm)	5	3.0%	4	2.3%	2	1.4%

* None resulted in clinical sequelae.

Table 10.9 Abdominal X-ray Findings – Component Migration*

Abdominal X-ray – Component Migration	6 Month (N=139)		12 Months (N=139)		24 Months (N=122)	
	N	(%)	N	(%)	N	(%)
Component Migration (≥ 10mm)	2	1.4%	1	1.0%	1	1.0%

* None resulted in clinical sequelae.

Table 10.10 Endoleak Status According to Evaluation Interval

Type of Endoleak*	Evaluation Interval							
	1 Month (N=180)		6 Month (N=177)		12 Month (N=156)		24 Month (N=119)	
	N	(%)	N	(%)	N	(%)	N	(%)
Type 1	7	4%	3	2%	2	1%	3	3%
Type II	21	12%	19	11%	19	12%	16	13%
Type III	0	0%	0	0%	0	0%	0	0%
Type IV	0	0%	0	0%	0	0%	0	0%
Indeterminate	11	6%	14	7%	6	4%	5	4%
Total	39	22%	36	20%	27	17%	24	20%

*As defined by White GH, et. al. JES 1997 and 1998.

Table 10.11 Change in Aneurysm Size by Interval

Change in Aneurysm Size	1 Month to 6 Months (N=182)		1 Month to 12 Months (N=181)		1 Month to 24 Months (N=146)	
	N	(%)	N	(%)	N	(%)
Increase $\geq$ 5mm	5	3%	13	7%	21	14%
No Change	159	87%	142	79%	97	67%
Decrease $\leq$ 5mm	18	10%	26	14%	28	19%

Table 10.12 Aneurysm Diameter Change with and without Endoleaks at 12-Months

Aneurysm Change from 1 to 12 Months*	Patients		With Endoleak at 12 Months*		Without Endoleak at 12 Months*	
	N	(%)	N	(%)	N	(%)
Increase ($\geq$ 5mm)	10	7%	4	40%	6	60%
No Change	118	81%	19	16%	99	84%
Decrease ($\geq$ 5mm)	18	12%	2	11%	16	89%
Total	146	100%	25	17%	121	83%

* Only includes subjects with interpretable films (endoleak) and measurements of aneurysm change from 1 to 12 months.

Table 10.13 Aneurysm Diameter Change with and without Endoleaks at 24-Months*

Aneurysm Change from 1 to 24 Months*	Patients		With Endoleak at 24 Months*		Without Endoleak at 24 Months*	
	N	(%)	N	(%)	N	(%)
Increase (≥ 5mm)	15	13%	7	47%	8	53%
No Change	74	66%	10	14%	64	86%
Decrease (≥ 5mm)	23	21%	2	9%	21	91%
Total	112	100%	19	17%	93	83%

* P = 0.004 for aneurysm size change and endoleak.

** Only includes subjects with interpretable films (endoleak) and measurements of aneurysm change from 1 to 24 months.

Secondary interventions within the first and second year each were performed in 6% of the EXCLUDER Bifurcated Endoprostheses subjects as shown in Table 10.14. All interventions were catheter-based except for one surgical ligation. Subjects may have had a single intervention to address both an endoleak and an aneurysm enlargement. No other interventions were performed for any other reason, e.g., migration, limb occlusion, through 24 months.

Table 10.14 Interventions for Endoleak and Aneurysm Size Increases

Intervention	Post-procedure to 12 Months (N=235)		> 12 Months to 24 Months (N=203)	
	N	(%)	N	(%)
Number of Subjects with ≥ 1 Intervention	15	6%	12	6%
Treat an Endoleak:				
Embolization	15	6%	6	4%
Ligation	1	0.4%	0	0%
Conversion to Open Repair	0	0	0*	0%
Treat an Aneurysm Increase:				
Embolization	0	0%	5**	3%
Ligation	1	0.4%	0	0%
Conversion to Open Repair	0	0%	0*	0%

* Total of three conversions post 24 months.
** Five also had endoleak.

As described in Table 10.15, treatment of AAA with EXCLUDER Bifurcated Endoprosthesis compared to the control group demonstrated significant benefits in recovery and quality of life measures.

Table 10.15 Secondary Outcomes by Treatment Group

Secondary Outcomes	EXCLUDER Bifurcated Endoprostheseis	Control
Blood Loss (ml) Mean (range)*	310 (50 – 2160)	1590 (100 – 7000)
Procedure Transfusion (%)	14%	89%
Procedure Time (minutes) Mean (range)*	144 (51 – 320)	196 (67 – 420)
ICU Stay (%)	24%	87%
Hospital Length of Stay (days) Mean (range)*	2 (1 – 11)	9.8 (3 – 114)
Time to First Oral Intake (days) Mean (range)*	0.5 (0 – 2.1)	2.6 (0.07 – 9.5)
Time to Ambulation (days) Mean (range)*	1.0 (0 – 5.0)	2.6 (0 – 18)
Time to Return to Normal Activities Mean (days)*	42	92

* Statistically significant ($P < .0001$).

10.5 Evaluation of Gender Bias

Abdominal aortic aneurysm disease is uncommon in women (male:female disease ratio 3:1 to 6:1). When women have AAAs, they less frequently have surgery. EXCLUDER Bifurcated Endoprosthesis subjects exhibited no significant differences between males and females for survival and freedom from major adverse events.

As shown below in Table 10.16, the results for EBE subjects were comparable between males and females. Women did not have an increased rate of early or late adverse events or mortality in the pivotal study. Various safety and other outcomes were compared for males and females in each of the treatment groups.

Table 10.16 Safety Outcomes According to Gender and Treatment Group

Treatment Group/ 12-months Outcome	Males		Females	
	% rate	95% CI	% rate	95% CI
EBE Subjects:	N= 204		N=31	
Survival	94%	89 – 96%	97%	80 – 99.5%
Freedom From Major Adverse Events	66%	59 – 72%	70%	52 – 84%
Cumulative Major Adverse Events (per patient)*	0.8	0.7 – 0.9	0.4	0.2 – 0.6
Control Subjects:	N=73		N=26	
Survival	97%	89 – 99%	87%	67 – 96%
Freedom From Major Adverse Events	35%	25 – 47%	38%	22 – 58%
Cumulative Major Adverse Events (per patient)	1.7	1.3 – 2.1	1.8	1.3 – 2.4

* Statistically significant at P = 0.003

Table 10.17 Additional Outcomes According to Gender and Treatment Group

Treatment Group/ Outcome	Males N	Males %	Females N	Females %
EBE:	N = 173		N = 28	
Aneurysm enlargement (≥5mm) at 1-year	143	83%	23	82%
Endoleak at 1-year	26	15%	5	18%

11.0 Conclusions Drawn from the Studies

As compared to conventional open surgery, the clinical benefits of the EXCLUDER Bifurcated Endoprosthesis are a lower rate of major complications, reduced blood loss and blood replacement volume, reduced need for an ICU stay, shorter hospitalization and faster return to normal activities. The risks include procedure- and/or device-related phenomenon, which include but are not limited to endoleaks and increase in aneurysm size.

12.0 Panel Recommendation

The Excluder™ Bifurcated Endoprosthesis was presented to the Circulatory System Device Panel on September 9, 2002. The Panel recommended approving the device with conditions. The first condition was mandatory five-year follow-up on all the patients in the pivotal study cohort to assess the long-term safety and effectiveness of the device. The second condition was to re-review the information on the 40 postoperative CT scans that had been classified as "uninterpretable" at the time of the submission to determine if additional information was available concerning these data. The third condition was that the Instructions for Use should stress the sources of co-morbidities and mortality, and that the patient labeling or brochure should include this information as well to provide further information to the physicians and patients concerning these issues.

13.0 FDA Decision

FDA reviewed portions of the the premarket approval (PMA) application under the modular PMA process (M000014). All of the modules were incorporated into the review of the PMA (P020004).

FDA concurred with the Circulatory System Devices Panel recommendations of September 9, 2002. To address these conditions, W.L. Gore & Associates submitted: 1) a written concurrence to conduct the mandatory five-year follow-up study; 2) information on the 40 postoperative CT scans, which was reviewed by FDA and found acceptable; and 3) revised labeling to address the concerns raised by the panel, which was reviewed by FDA and found acceptable.

FDA also asked the sponsor to provide a clinical update to physicians on the performance of the device due to the number of problems which historically have occurred with these types of device. This condition is consistent with conditions of approval issued by FDA for other marketed endovascular graft devices. The sponsor also provided their written concurrence to provide a clinical update to physicians annually on the performance of the device.

On March 16, 2001 and May 8, 2002, the sponsor's manufacturing facilities were inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

FDA issued an approval order for P020004 on November 6, 2002.
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12.0 APPROVAL SPECIFICATIONS

Directions for Use:	See labeling
Hazards to Health from Use of the Device:	See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the Labeling
Post-approval Requirements, Restrictions:	See approval order.